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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,711	04/20/2001	Darwin J. Prockop	53844-5005	6580

7590            05/19/2004

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[REDACTED] EXAMINER

KELLY, ROBERT M

ART UNIT	PAPER NUMBER
	1632

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	09/839,711	PROCKOP ET AL.
	Examiner Robert M Kelly	Art Unit 1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 09 February 2004.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-16 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) <input type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413)
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	Paper No(s)/Mail Date. _____
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date <u>2/9/04</u> .	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
	6) <input type="checkbox"/> Other: _____

**DETAILED ACTION**

Applicant's response and amendment filed 9 February 2004 has been entered.

Claims 1, 5, 9, and 13-16 have been amended.

Claims 1-16 are pending and considered.

***Oath/Declaration***

In light of Applicant's Declaration and Power of Attorney, received 9 February 2004, the objections to the Oath/Declaration are withdrawn.

***Priority***

In light of Applicants amendments to the specification, the objections to the specification are withdrawn.

***Claim Rejections – 35 USC § 112***

In light of Applicant's amendments and arguments, the rejections of Claims 1-16 under 35 USC 112, second paragraph, have been withdrawn.

***Claim Rejections - 35 USC § 102***

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 4-6, 8-10, and 12-16 remain rejected under 35 U.S.C. 102(b) as being anticipated by Anklesaria, et al. "Engraftment of a clonal bone marrow stromal cell line *in vivo* stimulates hematopoietic recovery from total body irradiation" (1987) Proc. Natl. Acad. Sci.,

USA, 84: 7681-85, hereinafter referred as “Anklesaria ‘87” for reasons of record in the previous Office Action of 6 October 2003.

### **Response to Arguments**

Applicant’s arguments filed 9 February 2004 have been fully considered but they are not persuasive.

Applicant argues that Anklesaria discloses a cell line that has been transformed or immortalized and that, as such, the cells are not the primary cultured marrow stromal cells of the present invention. Furthermore, Applicant cites pages 9 and 15, where it is disclosed specifically that the cells “are administered to a mammal upon isolation or following a period of *in vitro* culture” and that the isolated marrow stromal cells are “cultured *in vitro* prior to transplantation” (Applicant’s response, p. 8).

This argument is not persuasive because the claims encompass these cells, which were isolated from a mammal, and the cells are cultured *in vitro* prior to transplantation. The Claims as instantly pending do not recite that the cells are primary cultured marrow stromal cells, as Applicant argues. Additionally, the claims as instantly pending do not recite how long they are cultured or under what conditions the cells are cultured.

Applicant further argues that because Anklesaria teaches selection for neomycin, the cells are not the cells of Applicant’s invention, and therefore they do not anticipate Applicant’s claims.

This argument is not persuasive because the pending claims do not have any such limitation that the cells are not cells, and therefore, the claims would encompass the invention of

Anklesaria. If Applicant wished to exclude any particular conditions or steps, such limitation may be added to the claims; however, such amendments to the claims may invite new rejections.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 3, 7, and 11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Anklesaria '87 as applied to Claims 1-2, 5-6, and 9-10 above, and further in view of U.S. Patent No. 5,635,386 to Palsson, et al., hereinafter referred to as "Palsson '386" for reasons of record in the previous Office Action of 6 October 2003.

**Response to Arguments**

Applicant's arguments filed 9 February 2004 have been fully considered but they are not persuasive.

Applicant argues that there exists (i) no suggestion or motivation to modify one of the references, or combine the two references; (ii) no reasonable expectation of success upon such combining or modification; and (iii) that the references do not teach all the limitations of the claims (Applicant's Response, p. 9).

Such arguments are not considered persuasive, in view of the Examiner's initial rejection, which provided motivation to modify Anklesaria's teachings with that of Palsson (Non-Final

rejection, “Moreover, one of skill in the art at the time the invention was made would have been motivated to modify the teachings of Anklesaria ’87 with that of Palsson ‘386, and use human cell lines in humans to obtain the benefit of rescuing humans exposed to radiation or enhance hematopoeisis”, pp. 4-5), and a reasonable expectation of success upon such modification (“Furthermore, the artisan would have had a reasonable expectation of success, as bone marrow transplantation was already known and the cultures taught by Palsson ‘386 were known to afford improved methods for bone marrow transplantation, which necessarily demonstrates that cell lines themselves may be used in bone marrow transplantation in humans”, Id.). Moreover, each of the references teaches all of the limitations of the claims (Id.).

Applicant further argues that neither Anklesaria nor Palsson suggest that the administration of an isolated marrow stromal cell, as described in the present application, would rescue a mammal from a lethal dose of total body irradiation.

Such arguments are not persuasive, as the rejection is not based on the disclosure of the present application, but on the claims themselves, which encompass the cells of Anklesaria and/or Palsson. Moreover, as stated in the prior rejection, the reason for the damage to the marrow is considered irrelevant to the claims, as the method is concerned with recovery, not with a method of damaging marrow (Office Action dated 6 October 2003, pp. 3-4). Lastly, it is apparent from Anklesaria that total body irradiation results in an ablation of the marrow and subsequent lack of hematopoietic regeneration (Anklesaria, INTRODUCTION), and that is a primary reason for the studies of Anklesaria, which shows recovery of the marrow after stromal cell engraftment.

Applicant further argues that Anklesaria does not teach the cells described in the specification, and Palsson does not correct the deficiency, because Palsson does not mention the use of isolated marrow stromal cells as described in the as-filed specification to be administered to a mammal for rescuing a mammal from total body irradiation.

Such arguments are not persuasive because again, the rejection is based on the claims, not upon the specification. Moreover, the teachings of Anklesaria do encompass isolated marrow stromal cells, isolated from a mouse and administered allogenically (Office Action dated 6 October 2003, p. 4), and Palsson does teach that such cells may be used for treating humans (Id.). It is noted that the references are not each required, individually, to each all the aspects of the claims, but the combination of the references must, under the aforementioned requirements, make obvious the claims.

Applicant further argues that the specification teaches the coculturing of the stromal cells with hematopoietic stem cells, and that armed with such teachings, Applicant's claims are not obvious or anticipated by either Anklesaria and/or Palsson.

Such arguments are not persuasive because again, the rejection is based on the claims, and not on the specification. As recited, Claims 3, 7, and 11 encompass only the following limitations:

Claim 3: administration of isolated marrow stromal cells from an allogenic donor to a human that has been irradiated, wherein the marrow stromal cells are administered immediately after isolation or after any period of *in vitro* culturing.

Claim 7: administration of isolated marrow stromal cells from an allogenic donor to a human, wherein the stromal cells are administered immediately upon isolation or after a period of *in vitro* culturing.

Claim 11: administration of isolated marrow stromal cells from an allogenic donor to an irradiated human, wherein the stromal cells are administered immediately upon isolation or after a period of *in vitro* culturing.

Hence, these cells can, optionally be cultured, by any method, for any period of time, and do not even need to be cultured.

Applicant further argues that Palsson does not teach restoring the hematopoietic system, and that as such, even in view of Anklesaria, the claims are not obviated.

Such arguments are not considered persuasive because Anklesaria teaches a general method of treating marrow damage with the intent of hematopoietic recovery (TITLE). Palsson, moreover, teaches an improved method for marrow transplantation (Office Action dated 6 October 2003, p. 5). Therefore, such use was already known in the art and Palsson extends Anklesaria's teachings to humans.

Applicant further argues that Anklesaria provides no reasonable expectation of success, because such cells are not of Applicant's invention. To wit, Applicant argues that Anklesaria, by using cell lines that have been transformed (with a neomycin resistance gene) would not obviate cells not so transformed.

Such arguments are not considered persuasuve, because the transformation of these cells with a neomycin selection gene is not indicative of the ability to regenerate the

hematopoetic linages. Moreover, the rejection is based on the claims, not upon the specification and the claims encompass such cells transformed with neomycin selection genes.

Applicant further argues that Palsson teaches the culturing of hematopoetic stem cells, and Anklesaria teaches neomycin-transformed and selected cells, and that, therefore, there would be no reasonable expectation of success for rescuing an animal from total body irradiation.

Such arguments are not considered persuasive because Anklesaria specifically teaches stromal cells encompassed by Applicant's claims being used for treating total body irradiation (INTRODUCTION). Again Palsson provides further evidence that such treatments can be similarly applied in the case of humans (Office Action dated 6 October 2003, pp. 4-5).

Lastly, Applicant argues that Anklesaria does not teach the primary cultures of Applicant's invention and Palsson does not correct this deficiency, and that therefore, they do not render the present invention obvious.

Such arguments are not considered persuasive, as the rejection is based on the claims and not Applicant's specification.

## **CONCLUSION**

Claims 1-16 are rejected for reasons of record as originally applied in the Office Action dated 6 October 2003.

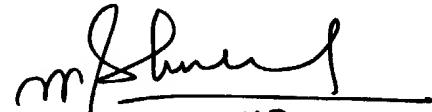
**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Art Unit: 1632

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE MONTH shorted statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert M Kelly whose telephone number is (571) 272-0729. The examiner can normally be reached on M-F, 9:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



RAM R. SHUKLA, PH.D.  
PRIMARY EXAMINER